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PRINCIPAL INVESTIGATOR: Marc D. Schwartz, Ph.D.

CONTRACTING ORGANIZATION: Georgetown University
Washington, DC 20057-1411

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Marc D. Schwartz, Ph.D.

E-Mail: schwartm@georgetown.edu

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

This project aims to gain a better understanding of the implications of genetic testing for breast-ovarian cancer susceptibility. The primary goal is to evaluate the impact of BRCA1/BRCA2 mutation testing on long term psychosocial (quality of life, distress, social functioning) and prevention/surveillance (mammography, CA125, transvaginal ultrasound, prophylactic mastectomy, prophylactic oophorectomy and chemoprevention) outcomes. To accomplish this we will measure outcomes within a group of women who received BRCA1/BRCA2 test results at least four years ago. We will divide our sample based upon their personal cancer history – evaluating cancer survivors with different measures compared to unaffected individuals. For both survivors and unaffected individuals we will recruit separate comparison samples of women who have never received BRCA1/BRCA2 testing. During this past year we received final approval from the DOD to begin accrual. We have initiated accrual and to date have completed follow-up interviews with xxx women. During the upcoming year we will continue accrual of our genetic testing cohort and will initiate accrual of our comparison groups.

15. SUBJECT TERMS
BRCA1, BRCA2, Outcomes

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INTRODUCTION

Genetic testing for breast-ovarian cancer susceptibility has the potential to reduce breast and ovarian cancer mortality among high risk women. However, there has been ongoing concern regarding the quality of life implications of learning one's mutation status. To date, there have been no studies to evaluate the long-term psychosocial and behavioral impact of receiving clinical BRCA1/2 test results. Several studies have examined these outcomes in the short-term. Although preliminary evidence suggests that the receipt of a positive BRCA1/2 test result does not lead to increased short-term distress, it is clear that women who receive positive test results do report more distress than those who receive negative test results. It is not clear, however, whether this distress has long-term implications. It is possible that distress could decline over time as the individual adapts to her positive test result and ongoing risk. Alternatively, the modestly elevated distress reported in the short-term could be evidence of chronic stress. Ongoing stress has been shown to adversely impact health behaviors and health outcomes. Given the risk status of this population, it is particularly important to better understand the long-term distress levels and the role of distress in adoption of recommended breast and ovarian cancer risk reduction and early detection behavior. To date, there have been no studies to examine these issues.

One of the main potential benefits of BRCA1/BRCA2 testing is to motivate carriers to take behavioral action to reduce their risk of breast and ovarian cancer mortality. However, we do not yet know whether carriers actually engage in such actions. Preliminary evidence suggests that a relatively small proportion of carriers obtain prophylactic surgery in the year following testing. The proportion of carriers who utilize chemopreventive agents such as tamoxifen remains unknown. The few studies to examine screening utilization in the year following disclosure found sub-optimal rates of screening among positives. In fact, rates of mammography have not been found to increase following a positive mutation test. Although mutation carriers did report higher rates of mammography, this difference was due to appropriate decreases in screening among younger noncarriers. In terms of ovarian cancer screening, rates of CA-125 and transvaginal ultrasound do increase among carriers in the year following testing. However, overall ovarian cancer screening rates remain below 30%. To date, there have been no studies to evaluate the long-term cancer prevention and screening behaviors of this population. If genetic testing is to fulfill its promise of reducing mortality among individuals from hereditary cancer families, behavioral change must follow the receipt of a positive test result. The first step to addressing this question is to evaluate the behavior of individuals in the years following testing. If individuals remain non-adherent to prevention and screening guidelines, it is particularly important to understand why and to identify early predictors of behavioral non-adherence in this vulnerable population. We will evaluate the role of distress/quality of life as a potential predictor of adverse behavioral outcomes.

The primary goal of this project is to evaluate long term psychosocial (quality of life, distress, social functioning) and prevention/surveillance (mammography, CA125, transvaginal ultrasound, prophylactic mastectomy, prophylactic oophorectomy and chemoprevention) outcomes. To accomplish this we will measure outcomes within a group of women who received BRCA1/BRCA2 test results at least four years ago. We will divide our sample based upon their personal cancer history – evaluating cancer survivors with different measures compared to unaffected individuals. For both survivors and unaffected individuals we will recruit separate comparison samples of women who have never received BRCA1/BRCA2 testing.

Until we better understand the long-term outcomes of BRCA1/2 testing, it is unlikely that such testing will fulfill its promise to reduce breast and ovarian cancer mortality. By evaluating the impact of

testing, appropriate intervention strategies can be developed so that individuals at-risk for distress or non-adherence could be targeted for early intervention and/or ongoing support. This research could provide information necessary to make decisions about how and where to allocate scarce counseling resources and to tailor health promotion efforts to individual needs. Genetic testing for breast-ovarian cancer susceptibility is becoming more widely available to the general population. Prior to its routine use, we should make sure that we fully understand its long-term implications.

BODY

We have listed each of the tasks from our Statement of Work, and the associated accomplishments.

Task 1. Finalize accrual procedures and measures to be included (months 1-6).

a. Meet with CARE program staff to confirm the procedures for patient recontact.

We completed this task during year 1.

b. Finalize recruitment letters for each of the study cohorts.

These letters were completed during year 1 and were included with the Year 1 Annual Report.

c. Finalize the telephone questionnaires to be administered to each cohort.

These interviews were completed during Year 1, were approved by the DOD IRB, and were included in the Year 1 Annual Report.

d. Develop interview database.

The study database was completed during Year 1, tested in Years 1 and 2, and became fully operational during Year 2. We are now using the database for all data entry and participant tracking. During Year 4 we will make slight modifications to the database to accommodate accrual of comparison participants.

e. Develop subject tracking system using Access database.

The tracking system has been developed and is currently being utilized for participant tracking.

f. Review computer databases of each cohort to determine procedures for participants recruitment and eligibility.

Done.

Task 2. Conduct participant accrual (months 4-48).

Participant accrual is ongoing. To date, we completed 328 interviews with former CARE participants. Thus far, just over 70% of eligible women have completed an interview. In addition to the 328 interviews that have been completed, we currently have 38 interviews scheduled and 50 participants who have agreed to participate, but have not yet scheduled their interview. Assuming 100% completion of the scheduled interviews and 60% completion of the interviews that have been consented to but not yet scheduled, we expect to have approximately 400 interviews completed by Sept 1. In addition, we currently have 50 individuals who are pending contact. Assuming our ongoing 70% completion rate, we should have an additional 35 interviews completed within the next 2-3 months. During the upcoming year, we will continue to contact past CARE participants as they become eligible. We expect to enroll at least another 150 former CARE participants during this year. Thus, by the conclusion of Year 4, we expect to have 450-550 completed cohort interviews.

During Year 3, we have also initiated comparison group accrual. We have delayed our comparison group accrual so that we can more accurately frequency match our comparison group to our cohort participants. Further, during Year 3 we focused on meeting our accrual goal of reaching 400 cohort participants. During Years 4 and 5 (no-cost extension year), we will increasingly focus on comparison group accrual. We expect our cohort enrollment to be completed by the end of Year 4. We will continue comparison enrollment into the no-cost extension year. To date, we have prepared initial mailings for 200 comparison group participants. These mailings will be sent out by Sept 1. Thus, we expect to complete our first comparison group interviews by Sept 15. We also have validated contact information for an additional 200 comparison group participants. We expect to initiate contact with these individuals by Winter 2007.

Despite initial delays, we expect to reach our projected sample sizes. We are close to reaching our proposed cohort sample of 500. Although we expect to reach that number shortly, we will need to recruit more than 500 cohort participants in order to maximize the number of unaffected participants in the study. Thus, by the middle of Year 4, we expect our accrual efforts to be primarily targeted at unaffected individuals.

Task 3. Preliminary Data Analyses (months 24-33)

We had originally proposed to begin preliminary data analyses at the start of Year 3. However, due to initial delays in approval of the protocol, we have had to delay preliminary analysis of data. Preliminary data analysis has recently begun on two research questions. First, we are examining the communication of genetic test results among individuals who underwent BRCA1/2 testing. Specifically, we are analyzing the association between communication with family members and long-term quality of life outcomes. We expect to submit a manuscript based upon this analysis in the Fall of 2006. We have also begun to analyze our data related to menopausal symptoms among women who underwent BRCA1/2 testing. We expect that these analyses will be completed and a manuscript submitted in Early Winter of 2007. Preliminary analyses will continue throughout Year 4.

Task 4. Final analysis and manuscript preparation (months 34-48).

We will begin to conduct our final analyses during the expected no-cost extension year.

KEY RESEARCH ACCOMPLISHMENTS

Our accomplishments during this year include the completion of over 250 participant interviews – to bring our total to 325. In addition, we have about 75 participant interviews pending – to bring our projected total to 400. Also during this past year, we have initiated our comparison group accrual. We have prepared initial mailing packets for the first wave of comparison interviews. We will initiate interviewing of this group by Sept 15 and we expect to complete up to 200 comparison group interviews during the upcoming 12-month period. Finally, we have initiated preliminary data analyses focused on questions related to family communication and menopausal symptoms/Hormone replacement utilization in our cohort sample. We expect to submit abstracts and manuscripts related to these issues during the upcoming 12-months of the award.

REPORTABLE OUTCOMES

To date we have no reportable outcomes.

CONCLUSIONS

This project seeks to gain a better understanding of the long-term psychosocial and behavioral implications of undergoing genetic counseling and testing for breast-ovarian cancer susceptibility. Since the start of the study, we have prepared all of our data collection and data management tools, hired our study staff, begun regular meetings, and compiled lists of participants to be contacted for participation. However, due to delays on the part of the Department of Defense Human Subjects review, we have been unable to commence study accrual and interviewing. After receiving final DOD approval, we initiated accrual and have been completing interviews at the expected pace.

REFERENCES

None

APPENDICES

A. Study Personnel Listing…

APPENDIX A: Current Salaried Study Personnel

Marc D. Schwartz, Ph.D.	Principal Investigator
Beth N. Peshkin, M.S.	Co-Investigator
Kathryn L. Taylor, Ph.D.	Co-Investigator
Claudine Isaacs, M.D.	Co-Investigator
Kristi Graves, Ph.D.	Project Director
Christy Gell, M.S.	Data Specialist
Sharon Hecker	Research Assistant
Shibao Feng, Ph.D.	Biostatistician